Chronic hepatitis in United Kingdom blood donors infected with hepatitis C virus

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Chronic hepatitis in United Kingdom blood donors infected with hepatitis C virus

W L Irving, K R Neal, J C E Underwood, P N Simmonds, V James, on behalf of Trent Regional Hepatitis C Virus Study Group

University Hospital, Queen's Medical Centre, Nottingham NG7 2UH
W L Irving, *senior lecturer in clinical virology*
K R Neal, *lecturer in public health medicine and epidemiology*

Royal Hallamshire Hospital, Sheffield S10 2JF
J C E Underwood, *professor of pathology*

Medical School, University of Edinburgh, Edinburgh EH8 9AG
P N Simmonds, *lecturer in medical microbiology*

Trent Regional Blood Transfusion Centre, Sheffield S5 7JN
V James, *consultant haematologist*

Other members of the Trent Regional Hepatitis C Virus Study Group are listed at the end of the paper.

Correspondence to:
Dr Irving.

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Routine screening for antibodies to hepatitis C virus in blood donations was introduced in Britain in 1991. It showed that 1 in 2000 donors was positive for antibodies. The natural course and importance of hepatitis C virus infection in apparently healthy people are unclear. We assessed the value of clinical and laboratory data in predicting the need for liver biopsy in blood donors with antibodies to hepatitis C virus.

Patients, methods, and results

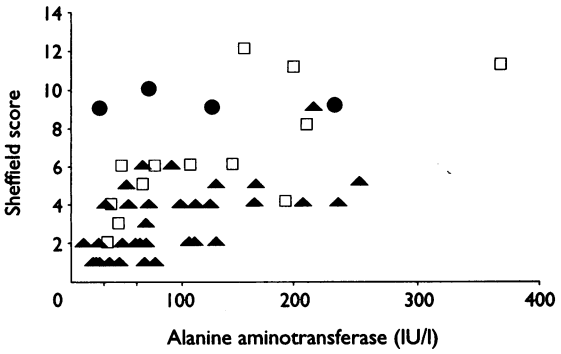
Blood donors in the Trent region are screened for antibodies to hepatitis C virus by second generation enzyme linked immunosorbent assay, and results are confirmed by a four antigen recombinant immunoblot assay. Donors with positive results are interviewed and referred to a consultant for further management. We studied all 52 donors who had had a liver biopsy by 1 May 1993 (30 men, 22 women; aged 21-57 (mean 35) years).

We collected data on risk factors for hepatitis C virus infection, duration of infection (assuming that infection was acquired on the first exposure to a risk factor), and alcohol intake. Alanine aminotransferase concentrations (three measurements), GOR antibodies,[1] hepatitis C virus RNA,[2] and hepatitis C virus serotype[3] were measured. Biopsy specimens were scored blind by the Knodell and Sheffield[4] schemes; the Sheffield scheme includes assessment of histological features characteristic of hepatitis C. We used the statistical package SPSS-PC to analyse data with Spearman rank correlation, Mann-Whitney, and logistic regression analyses. Predictive values for severe liver disease (chronic active hepatitis or cirrhosis) were calculated by using the standard definition and 95% confidence intervals by the program Confidence Interval Analysis.

The histological diagnoses were cirrhosis (four patients), chronic active hepatitis (13), chronic persistent hepatitis (32), fatty change (one), and normal (two). Hepatitis C virus RNA was detected in sera from 51 donors. The biopsy specimen from the donor without viral RNA was normal. Hepatitis C virus RNA was assayed twice in 31 donors: 28 had positive results in both samples, one had negative results in both, and two had a positive result in the first sample but a negative second result. The biopsy specimens from the donors with discordant results were reported as normal in one and chronic persistent hepatitis with features of α_1 antitrypsin deficiency in the other. A negative test result was significantly associated with lower severity scores for biopsy specimens (Knodell score $P=0{\cdot}006$; Sheffield score $P=0{\cdot}005$).

Peak alanine aminotransferase concentration was correlated with both severity scores (Knodell score $r_s=0{\cdot}59$, $P<0{\cdot}001$; Sheffield score $r_s=0{\cdot}66$, $p<0{\cdot}001$, figure). The predictive value for chronic active hepatitis or cirrhosis was 0·42 (13/31 donors, 95% confidence interval 0·25 to 0·61) for an alanine aminotransferase concentration above 60 IU/l and 0·47 (9/19, 0·24 to 0·71) for a concentration above 100 IU/l. The predictive value of an alanine aminotransferase concentration under 60 IU/l for chronic persistent hepatitis, fatty change, or a normal biopsy result was 0·81 (17/21, 0·58 to 0·95).

Liver damage was more severe in men than women (median Knodell score 4 *v* 2, $P=0{\cdot}03$; Sheffield score 5 *v* 3, $P=0{\cdot}02$). Logistic regression models found no other significant predictor for histological change.



Correlation between Sheffield score of severity of disease in liver biopsy specimen and peak alanine aminotransferase concentration.
▲=*Chronic hepatitis or normal,* ●=*cirrhosis,* □=*chronic active hepatitis*

Comment

Fifty of 52 biopsy specimens from apparently healthy blood donors infected with hepatitis C virus were abnormal, with a third having evidence of chronic active hepatitis or cirrhosis. Although peak alanine aminotransferase concentration and biopsy scores were strongly correlated, alanine aminotransferase concentration was a poor predictor of serious liver disease.

Possible explanations for the discordant results with the test for hepatitis C virus RNA include intermittent viraemia,[5] low level viraemia, false positive or negative results, and clearance of viraemia between sampling. Larger studies are needed to determine whether variable results for viral RNA are associated with less severe liver disease.

We found no useful predictors of the severity of liver disease. Our estimates of age at, and duration of, infection, however, had obvious limitations. Our data suggest that donors who have repeated positive results for hepatitis C virus RNA require liver biopsy as a large proportion will have serious liver disease that cannot be predicted by measuring alanine aminotransferase concentration.

Members of the Trent Regional Hepatitis C Virus Study Group were D A Jones, P Nuttall (Trent Regional Blood Transfusion Service); S Day (Nottingham University); D

Bennett, R P Eglin (Leeds Public Health Laboratory); R G Finch, R Read (Nottingham City Hospital); M McKendrick, D R Triger, D Williams (Royal Hallamshire Hospital, Sheffield); B B Scott (Lincoln County Hospital); K G Nicholson, M Wiselka (Leicester Royal Infirmary); J Freeman (Derby Royal Infirmary), and K Rose (Department of Microbiology, University of Edinburgh).

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Follow up of blood donors positive for antibodies to hepatitis C virus

Kate E Ryan, Sheila MacLennan, J A J Barbara, Patricia E Hewitt

North London Blood Transfusion Centre, Colindale, London NW9 5BG
Kate E Ryan, *senior registrar*
Sheila MacLennan, *senior registrar*
J A J Barbara, *head of microbiology*
Patricia E Hewitt, *deputy medical director*

Correspondence to:
Dr Hewitt.

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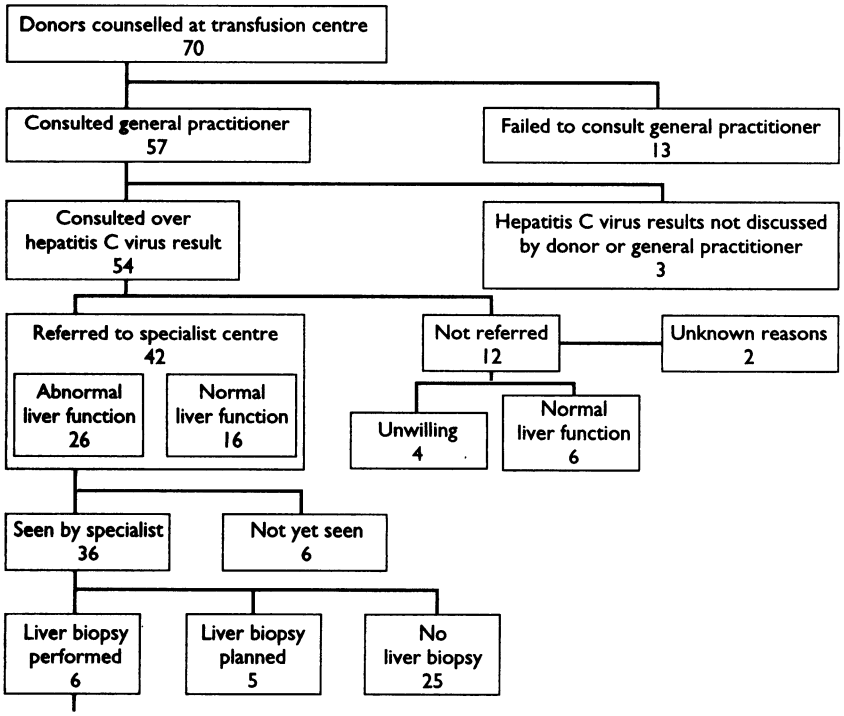
The hepatitis C virus has been identified as the main cause of post-transfusion hepatitis.[1] Mandatory screening of blood donations for antibodies to hepatitis C virus was introduced by the National Blood Transfusion Service on 1 September 1991. Donors confirmed to be positive for antibodies to hepatitis C virus at the North London Blood Transfusion Centre are offered counselling by medical staff at the centre, who explain the relevance of the test results. They are then referred to their general practitioner.

Current evidence suggests that many of the asymptomatic donors positive for antibodies to hepatitis C virus are chronic carriers, in whom the virus replicates.[2] Probably some asymptomatic donors will progress to clinically significant, and possibly severe, liver disease in the future. Follow up of the donor by the general practitioner or hospital clinic, or both, will be influenced by information and advice given as a result of the initial counselling. To date there has been no information on the effectiveness of the counselling procedure and the fate of donors after leaving the transfusion centre. We carried out a postal survey on the follow up arrangements for blood donors positive for antibodies to hepatitis C virus.



Flow chart showing management of anti-HCV positive blood donors

Subjects, methods, and results

A postal questionnaire was sent to 83 of 107 blood donors positive for antibodies to hepatitis C virus who had been identified and counselled at the North London Blood Transfusion Centre until the end of June 1992. The remaining donors were excluded either because they had failed to attend for counselling (16 donors) or because they were uncontactable (eight donors). A questionnaire was then sent to the doctors of 80 of these donors (two donors withheld consent and in one case the general practitioner was unknown). Replies were received from 50 donors and 61 general practitioners (response rates 60% and 76% respectively). Taken together, the questionnaire responses gave information on 70 donors. Presentation of the donor to the general practitioner and subsequent management by the general practitioner are shown in the flow chart. The demographic details and possible sources of infection of these donors have been analysed separately.[3]

Most of the donors positive for antibodies to hepatitis C virus were referred for specialist opinion irrespective of whether their liver function was reported as abnormal by the transfusion centre. Of the 12 donors not referred, four either refused or failed to attend follow up appointments with the general practitioner and six had normal liver function values; lack of referral was in accordance with the centre's guidelines at the time. Liver biopsy was performed or pending in 11 cases. One donor had been considered for treatment with interferon alfa after the biopsy result.

The partners (all heterosexual) of 27 donors were tested. None of 14 male partners and one of 13 female partners was found to be infected, but details of possible shared risk factors for this partner were not available. Overall, general practitioners and donors indicated satisfaction with the counselling service at the transfusion centre. The main concerns expressed by donors were implications for sexual partners and for future offspring.

Comment

The positivity rate positive for antibodies to hepatitis C virus among first time donors at the North London Blood Transfusion Centre is one in 1400. Based on these figures, we should anticipate that 30 such asymptomatic subjects would be identified annually at the centre once the established donor panel had been screened.

This survey shows that, after counselling, 13 of 70 donors did not consult their general practitioner about their hepatitis C virus result. Of those who do, however, most are being referred to a specialist clinic